

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB2005/000811

A. CLASSIFICATION OF SUBJECT MATTER
INV. C12N15/62 C12N15/87 A61K47/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C12N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| X | VOORHOEVE P M ET AL: "Knockdown stands up" TRENDS IN BIOTECHNOLOGY, ELSEVIER PUBLICATIONS, CAMBRIDGE, GB, vol. 21, no. 1, January 2003 (2003-01), pages 2-4, XP004397628 ISSN: 0167-7799 page 3, right-hand column ----- -/-/ | 1-29 |

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the International filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the International filing date but later than the priority date claimed

- "T" later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

19 October 2006

Date of mailing of the International search report

26-02-2007

Name and mailing address of the ISA

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| X | <p>MINAMISAWA SUSUMU ET AL: "Chronic phospholamban-sarcoplasmic reticulum calcium ATPase interaction is the critical calcium cycling defect in dilated cardiomyopathy"</p> <p>CELL, CELL PRESS, CAMBRIDGE, MA, US, vol. 99, no. 3, 29 October 1999 (1999-10-29), pages 313-322, XP002139385 ISSN: 0092-8674 page 319, right-hand column</p> <p>-----</p> <p>LUNDGREN JOSEFIN ET AL: "Use of RNA interference and complementation to study the function of the Drosophila and human 26S proteasome subunit S13."</p> <p>MOLECULAR AND CELLULAR BIOLOGY, vol. 23, no. 15, August 2003 (2003-08), pages 5320-5330, XP002403680 ISSN: 0270-7306 abstract page 5321, left-hand column - right-hand column page 5325, right-hand column - page 5327, left-hand column</p> <p>-----</p> <p>MAO YINGWEI & LEE ANGEL W: "Gab2 functions in IL-3- and basic FGF-mediated cell survival."</p> <p>45TH ANNUAL MEETING OF THE AMERICAN SOCIETY OF HEMATOLOGY; SAN DIEGO, CA, US, [Online] 6 December 2003 (2003-12-06), XP002403681 Retrieved from the Internet: URL:http://www.abstracts2view.com/hem/view.php?nu=HEM3L1_5020> [retrieved on 2006-10-06] abstract 1286 the whole document & BLOOD, vol. 102, no. 11, 16 November 2003 (2003-11-16), page 355a, & 45TH ANNUAL MEETING OF THE AMERICAN SOCIETY OF HEMATOLOGY; SAN DIEGO, CA, USA; DECEMBER 06-09, 2003 ISSN: 0006-4971</p> <p>-----</p> <p>-/-</p> | 1-29 |
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| X | | 1-29 |

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|----------|---|-----------------------|
| Y | DAVIS B G ET AL: "Selective protein degradation by ligand-targeted enzymes: towards the creation of catalytic antagonists" CHEMBIOCHEM - A EUROPEAN JOURNAL OF CHEMICAL BIOLOGY, WILEY VCH, WEINHEIM, DE, vol. 4, no. 6, 6 June 2003 (2003-06-06), pages 533-537, XP002379393 ISSN: 1439-4227 cited in the application the whole document ----- | 1-29 |
| Y | HOSHIJIMA MASAHIKO ET AL: "Chronic suppression of heart-failure progression by a pseudophosphorylated mutant of phospholamban via in vivo cardiac rAAV gene delivery" NATURE MEDICINE, NATURE PUBLISHING GROUP, NEW YORK, NY, US, vol. 8, no. 8, August 2002 (2002-08), pages 864-871, XP002303162 ISSN: 1078-8956 the whole document ----- | 1-29 |
| Y | MIYAKI MICHYIKO ET AL: "Increased cell-substratum adhesion, and decreased gelatinase secretion and cell growth, induced by E-cadherin transfection of human colon carcinoma cells" ONCOGENE, vol. 11, no. 12, 1995, pages 2547-2552, XP008068358 ISSN: 0950-9232 abstract page 2547, right-hand column, paragraph RESULTS - page 2550, left-hand column, paragraph 1 ----- | 1-29 |
| A | FUKUDA K: "Apoptosis-associated cleavage of [beta]-catenin in human colon cancer and rat hepatoma cells" INTERNATIONAL JOURNAL OF BIOCHEMISTRY AND CELL BIOLOGY 1999 UNITED KINGDOM, vol. 31, no. 3-4, 1999, pages 519-529, XP002403682 ISSN: 1357-2725 the whole document ----- -/- | 1-29 |

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|----------|---|-----------------------|
| A | KOVACS R J ET AL: "Phospholamban forms Ca ₂₊ -selective channels in lipid bilayers" JOURNAL OF BIOLOGICAL CHEMISTRY 1988 UNITED STATES, vol. 263, no. 34, 1988, pages 18364-18368, XP002403683 ISSN: 0021-9258 the whole document ----- | 1-29 |

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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 1-9 are directed to a method of treatment of the human/animal body, a search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

see annex

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-12

Method of replacing an adverse target moiety by its non-adverse homologue, and products to be used in this method.

1.1. claims: 1-9 in part, and 10

Method of replacing an adverse target moiety by its non-adverse homologue, and products to be used in this method, wherein the targeting module comprises a beta-catenin binding domain of E-cadherin.

1.2. claims: 1-9 in part, and 11

Method of replacing an adverse target moiety by its non-adverse homologue, and products to be used in this method, wherein the targeting module comprises an inhibitor of ADH.

1.3. claims: 1-9 in part, and 12

Method of replacing an adverse target moiety by its non-adverse homologue, and products to be used in this method, wherein the targeting module comprises a PLB target motif.

2. claims: 13-29

Nucleic acid encoding a specific form of PLB, method for producing it, and its use as defined in these claims.
